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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/258,031	02/25/1999	MAARTEN HUBERTUS STUIVER	U-012121-2	3286

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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 06/21/2002

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/258,031

Applicant(s)

STUIVER ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2001.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-10, 12-38, 42-44 and 46-63 is/are pending in the application.
- 4a) Of the above claim(s) 7-10, 12-38, 42-44 and 46-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 51-53, 55-58 and 61-63 is/are rejected.
- 7) ☒ Claim(s) 54 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Continued Prosecution Application

The request filed on 10/24/2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/258,031 is acceptable and a CPA has been established. An action on the CPA follows.

Applicants have checked the box of the request for a CPA indicating that no amendment was filed with this request, thus the claims remain the same and all of the rejections of record are maintained for the reasons of record.

Claims 7-10, 12-38, 42-44, and 46-63 are currently pending and present for examination.

Claims 7-10, 12-38, 42-44 and 46-50 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

Claim 54 is objected to because of the following informalities: Claim 54 is dependent on.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 51, 52, 53, 55, 56, 57, 58 and 61-63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was presented originally in a previous office action for claims 1-6, 11, 39-41 and 45, now canceled.

Claims 51, 52, 53, 55, 56, 57, 58 and 61-63 are directed to all possible proteins or compositions comprising an amino acid sequence encoded by SEQ ID NO 15 and having an antifungal activity; **or a mutein of the amino acid sequence encoded by SEQ ID NO: 15 having sufficient identity to the amino acid sequence of SEQ ID NO: 15 to retain the antifungal activity of the amino acid sequence of SEQ ID NO: 15**; or a part of the amino acid sequence of SEQ ID NO: 15 having antifungal activity;...(claim 51 and 55), wherein said protein naturally occurs in sunflower or lettuce (claim 52), wherein said protein has anti-Oomycete activity or anti-Phytophthora activity or anti-Pythium activity or a combination thereof (claim 53) Claim 56 is directed to **any** naturally occurring plant protein having carbohydrate oxidase activity and antifungal activity. Claim 57 is directed to all possible carbohydrate oxidases comprising an amino acid sequence of SEQ ID NO 16 and having an antifungal activity; **or a mutein of the amino acid sequence encoded by SEQ ID NO: 16 having sufficient identity to the amino acid sequence of SEQ ID NO: 16 to retain the antifungal activity of the amino acid sequence of SEQ ID NO: 16**; or a part of the amino acid sequence of SEQ ID NO: 16 having antifungal activity;... Claim 58 is directed to all possible antifungal proteins comprising the amino acid sequence of amino acids 1 to 25 of SEQ ID NO: 1,

amino acids 1 to 25 of SEQ ID NO: 2, amino acids 1 to 118 of SEQ ID NO: 6, amino acids 1 to 529 of SEQ ID NO: 16, amino acids 1 to 529 of SEQ ID NO: 20 **or a mutein of the said amino acid sequence of SEQ ID NOs: 1, 2, 6, 16, or 20 having sufficient identity to the amino acid sequence of SEQ ID NOs: 1, 2, 6, 16, or 20 to retain the antifungal activity of the protein;**... Claims 61-63 are directed to **any** naturally occurring plant protein having carbohydrate oxidase activity and a molecular weight of 55-65kD (claim 61), wherein said protein is a hexose oxidase (claim 62), wherein said protein is from sunflower or lettuce (claim 63).

As discussed in a previous office action, the specification only provides representative species from sunflower, lettuce and *arabidopsis* encompassed by these claims. There is no disclosure of any particular **structure to function/activity** relationship in the disclosed species. The specification also fails to describe additional representative species of these proteins by any identifying structural characteristics or properties other than the carbohydrate oxidase activity and antifungal activity, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would not recognize Applicants were in possession of the claimed invention.

Applicants traversed this rejection as it applied to claims 1-6, 11, 39-41 and 45, on the basis applicants have satisfied the written description requirement by sufficient description of a representative number of species. Applicants have amended the subject claims such that they are limited to muteins that have sufficient identity to the amino acid sequences of the described species such that they retain antifungal activity thereof. This argument is not found persuasive. While it is not necessary to provide individual support for each species that the genus embraces, this can be overcome by

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sufficient description of a representative number of species of the claimed genus. As discussed above and in the previous office action applicants have not presented a sufficient number of species of the claimed genus. The requirement of written description may also be met by the disclosure of identifying characteristics such as partial structure, physical and/or chemical properties, functional characteristics, correlation between structure and function method of making and combinations of these. Applicants have not adequately described the claimed genus. Applicants further present Example 14 of the Examiner Training Materials issued in connection with the Revised Description Guidelines in support of their argument. It is pointed out that in this example the claim contains both structure ("having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3") and function limitations ("catalyze the reaction of A B"). Applicants claims as currently amended do not have such a structural limitation thus it is unclear how applicants believe this example supports their assertion. Applicants claims that recite a mutein of the amino acid sequence encoded by SEQ ID NO: X having sufficient identity to the amino acid sequence of SEQ ID NO: X to retain antifungal activity of the amino acid sequence of SEQ ID NO: X has no structural limitation, and thus any protein with antifungal activity that comprises a single amino acid in common with SEQ ID NO: X, such as alanine, is encompassed by this claim.

Applicants further assert that the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. As discussed above and in the previous office action, applicants have only disclosed the claimed carbohydrate oxidase and having a molecular weight of 55-65kD from sunflower, lettuce and *arabidopsis*. This is not representative of the genus of molecules drawn to all naturally

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occurring carbohydrate oxidase having a molecular weight of 55-65kD from any plant. Further, as discussed above with respect to meeting the requirements necessary to meet the written description requirement as discussed above the specification is lacking.

Claims 51, 52, 53, 55, 56, 57, 58 and 61-63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those carbohydrate oxidase proteins having antifungal activity wherein the proteins are encoded by the nucleotide sequence as shown in SEQ ID NOs: 15, 19, or comprising peptides selected from the group consisting of SEQ ID NOs: 1, 2, 6, 16 and 20, does not reasonably provide enablement for any protein having carbohydrate oxidase or antifungal activity, wherein said protein is encoded by a specific nucleotide sequence as claimed or parts or **muteins** thereof having sufficient identity to the original amino acid sequence to retain the activity of the original, or antifungal compositions comprising said proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in a previous office action as it applies to claims 1-6, 11, 39-41 and 45.

Applicants have traversed this rejection on the basis that the currently "applicable claims have been limited to muteins that have a substantial identity with the specific sequences described in the specification" and such mutein can be routinely tested according to methods described in the specification and therefore the experimentation needed to practice the invention as claimed cannot be considered to be "undue". This argument is not found persuasive for a number of reasons. First, the claims have been limited to muteins that have **sufficient identity to the specific SEQ ID NO to retain**

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antifungal activity, not “substantial identity” to the specific SEQ ID NOs and even if the claims included the limitation of having “substantial identity” to specific SEQ ID NOs, a structural definition of a protein based on “substantial identity” to the a specific SEQ ID NOs is somewhat unclear and indefinite. A clear limitation of the claimed subject matter to those proteins with structural similarity to SEQ ID NOs... such as proteins which are encoded by DNAs which will hybridize to SEQ ID NOs... under specific conditions or to % identity would overcome this rejection. Second, Applicants argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because the specification teaches the complete nucleotide and amino acid sequences of the claimed proteins and methods for producing variants of a disclosed sequence are within the skill of the ordinary artisan. This is not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., maintaining antifungal activity) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting antifungal and/or carbohydrate oxidase activity and thermostability; (B) the general tolerance of these proteins to modification and extent of such tolerance; (C) a rational

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and predictable scheme for modifying any of these proteins with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

With respect to those claims reciting that the recited proteins occur naturally in plants, applicants give no structural limitations other than having a specific molecular weight and/or having antifungal or carbohydrate oxidase activity and thus the identification and isolation of such proteins based solely on these activities and this limited structural information from all species of plants clearly would entail undue experimentation. Applicant is reminded that the claims as presently amended, for instance the recitation of claim 51 "**a mutein of the amino acid sequence encoded by SEQ ID NO: 15 having sufficient identity to the amino acid sequence of SEQ ID NO: 15 to retain the antifungal activity of the amino acid sequence of SEQ ID NO: 15**" reads on any protein having antifungal activity and thus applicants have given insufficient structural guidance to allow one of ordinary skill in the art to isolate, identify or make the claimed proteins.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 51, 55, 56, 57, 58 are rejected under 35 U.S.C. 102(a) as being anticipated by Stougaard et al. (WO 96/40935).

Stougaard et al. teach a method of producing recombinantly a hexose oxidase from a number of different marine algal species for use as an antimicrobial agent. Specifically, Stougaard et al. teach the use of hexose oxidase as expressed in silage inoculants to deplete oxygen thereby inhibiting the growth of aerobic spoilage organisms such as gram negative bacteria and yeasts (page 16, lines 12-32).

Therefore, Stougaard et al. anticipates claims 51, 55, 56, 57, 58, drawn to an isolated protein which has antifungal activity, carbohydrate oxidase activity, which is obtainable from a plant source encoded by the nucleotide sequence shown in SEQ ID NO: 15 or a **mutein of the amino acid sequence encoded by SEQ ID NO: 15 having sufficient identity to the amino acid sequence of SEQ ID NO: 15 to retain the antifungal activity of the amino acid sequence of SEQ ID NO: 15**(See discussion above for interpretation of this bolded phrase) and an antifungal composition containing said protein.

Claims 51, 53, 55, 57 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Hu et al. (Plant Molecular Biology 34: 949-959, Aug 1997).

Hu et al. teach the cloning and expression of a PR5-like protein from *Arabidopsis*, its expression in *E. coli* and its use to inhibit fungal growth as part of a composition.

Therefore Hu et al. anticipates claims 51, 53, 55, 57 and 58.

Claims 51, 53, 55, 57 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Woloshuk et al. (Plant Cell 3: 619-628, June 1991).

Woloshuk et al. teach that the cell walls of most fungi in the taxonomic class Oomycetes have a b-1,3-glucan component but contain no chitin, thus the *Oomycetes*

Phytophthora cactorum, *Pythium ultimum*, and *Pythium aphanidermatum* have been shown to be insensitive to a mixture of chitinase and b-1,3-glucanase. Woloshuk et al. further hypothesize that factors other than chitinase and b-1,3-glucanase are involved in induced resistance against this class of pathogens. Woloshuk et al. teach a bioassay using *P. infestans* for the identification of the factors involved in the resistance to this agronomically important pathogen. Woloshuk et al. further identified, purified and characterized a protein, AP24 from tobacco plants, which caused lysis of sporangia and inhibition of hyphal growth.

Therefore, Woloshuk et al. anticipates claims 51, 53, 55, 57 and 58.

Applicants traverse each of the above 102 art rejections on the basis that the examiner has not provided any explanation of where in the cited references, if at all, there appears a disclosure of the specific sequences covered by the recited SEQ ID NOs and that applicants believe that the rejections are based on the "expansive" reading of the term "muteins". Applicants assert that the claims have now been limited such that they cover only muteins having "substantial identity with the recited SEQ ID NOs and having the claimed antifungal activity. Applicants maintain that in the absence of a teaching in the references of the claimed sequences, that the rejection should be withdrawn. This argument is not found responsive, and as discussed above under the traversal of the 112 enablement rejection, the currently amended claims are not limited to "substantial identity" but to "sufficient identity to the specific SEQ ID NO to retain antifungal activity", and also as discussed above interpretation of "a mutein of the amino acid sequence encoded by SEQ ID NO: 15 having sufficient identity to the amino acid sequence of SEQ ID NO: 15 to retain the antifungal activity of the amino acid sequence of SEQ ID NO: 15" is that it encompasses any protein having antifungal activity.

Conclusion

This is a CPA of applicant's earlier Application No. 09/258,031. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

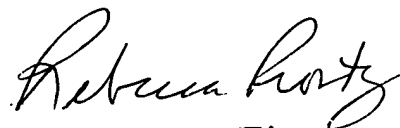
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax

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phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
June 20, 2002



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600